Influence of cholecystectomy on symptomatic cholelithiasis: can all symptoms be improved?

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ABSTRACT

Objective
To analyze the outcome of cholecystectomies in patients with symptomatic cholelithiasis for improvement in the pre-operative symptoms.

Methods
This cross-sectional interview-based prospective study included 200 patients who responded to a pre-designed questionnaire in a tertiary care hospital, seen from March 2007 through May 2009. They were interviewed in the post-operative period for improvement in their symptoms at intervals of 1, 3 and 6 months. The patients with common bile duct stones, bilio-enteric fistulae, carcinoma of gall bladder with cholelithiasis, and those lost to follow up were excluded from the study. A benefit ratio (BR) was calculated using SPSS v. 13 for each symptom. BR close to 1.0 was interpreted as evidence of gall stone disease related specifically to the symptom.

Results
Out of 200 patients, there were 142 females and 58 males. Mean age was 46.5 years (range 14-92, SD±14.25). 98.5% of patients had abdominal pain associated with gallstones. Other symptoms of variable frequency were nausea (70%), dyspepsia (58.5%), fatty food intolerance (57%), vomiting (25%), heartburn (24.5%) and flatulence (21%). After cholecystectomy, 98.5% patients had complete relief of abdominal pain and vomiting at 6 months (BR=1). Fatty food intolerance seen in 57% patients pre-operatively stayed at 7.5% at six months (BR=0.87). Dyspepsia persisted in 38.5% patients post-operatively (BR=0.34). De novo appearance of symptoms was noted in 5% of patients. 93.5% patients were satisfied with the outcome of surgery.

Conclusion
Cholecystectomy appears to relieve specifically biliary pain, nausea, vomiting and fatty
food intolerance associated with gallstone disease. Other abdominal symptoms that are non-specific like flatulence, dyspepsia and heartburn are only partly relieved. Despite the persistence or appearance of new symptoms, most patients were satisfied with the outcome of surgery. (Rawal Med J 2009;34: ).

**Keywords**
Cholelithiasis, cholecystectomy, symptoms, outcome.
INTRODUCTION
A wide variety of symptoms are associated with gallstones but not all of these are relieved after cholecystectomy, raising doubts whether these symptoms were, in fact, due to gallbladder dysfunction itself or due to certain other factors.\textsuperscript{1,2} It has also been observed that symptoms may arise de novo after an apparently successful cholecystectomy.\textsuperscript{3} These are referred to as ‘Post-cholecystectomy syndrome’.\textsuperscript{3,4} Studies have identified some of the causes for this symptom complex as disturbance of bile metabolism and entero-hepatic cycling due to loss of reservoir function of the gall bladder.\textsuperscript{4} The success of a procedure depends upon completion of the procedure without any complication and improvement in the symptoms for which the operation was planned. It is therefore prudent to know the patient’s perspective on improvement in symptoms for which the operation was done. This study was carried out to ascertain pre-operative symptoms associated with gallbladder stones and outcome of the removal of gall bladder for improvement in these symptoms or appearance of new symptoms during follow up period.

PATIENTS AND METHODS
The study was carried out between May 2007 and June 2008 at Shifa International Hospital, Islamabad and included 200 patients, who were interviewed using a pre-designed Performa during the post-operative period after cholecystectomy. Informed consent was taken from all patients. All of the patients had cholelithiasis confirmed on abdominal ultrasonography. All were operated by either laparoscopic cholecystectomy or mini-cholecystectomy. Besides demographics, patients were asked about the symptoms they had in the pre-operative period. They were then interviewed in the post-operative period for improvement in their symptoms at intervals of 1, 3 and 6 months. The patients were contacted mostly on telephone. The patients with common bile duct stones, bilio-enteric fistulae, carcinoma of gall bladder with cholelithiasis, and those lost to follow up were excluded from the study. Those who developed major complications after cholecystectomy, requiring prolonged hospitalization, such as biliary leak requiring hepatico-jejunostomy, pancreatitis, and major collections requiring laparotomy were also excluded from the study. All received three doses of antibiotic, usually cefuroxime 750 mg for peri-operative prophylaxis.
A benefit ratio (BR) was calculated for each symptom. A BR close to 1.0 was interpreted as evidence of gall stone disease related specifically to the symptom. Chi square $X^2$ test was used for statistical analysis using SPSS v. 13. $P$ value of $<0.05$ was considered significant. Unanswered questions were excluded from the final analysis.
RESULTS
Out of 200 patients, 142 were females and 58 males (M:F ratio 1:2.4). Mean age was 46.5 years (range 14-92, SD±14.25). As noted in table 1, 98.5% of patients had abdominal pain; 59.5% colicky and 39% nagging in nature. Other symptoms were of variable frequency (Table 1). After cholecystectomy, patients were followed at 1, 3 and 6 months intervals. As noted in the table 2, 98.5% patients had complete relief of abdominal pain at 6 months (BR=1). Vomiting persisted in 2% at one month but disappeared later (BR=1). Some patients, however, continued to experience nausea in the post-operative period (17.5% at one month, 12% at three months, and 9.5% at 6 months compared to 70% in the pre-operative period (BR=0.85).
Table 1. Preoperative symptoms and signs (N = 200).

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colicky abdominal pain</td>
<td>119</td>
<td>59.5</td>
</tr>
<tr>
<td>Nagging abdominal pain</td>
<td>78</td>
<td>39</td>
</tr>
<tr>
<td>Nausea</td>
<td>140</td>
<td>70</td>
</tr>
<tr>
<td>Vomiting</td>
<td>50</td>
<td>25</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>116</td>
<td>58</td>
</tr>
<tr>
<td>Fatty Food Intolerance</td>
<td>114</td>
<td>57</td>
</tr>
<tr>
<td>Flatulence</td>
<td>42</td>
<td>21</td>
</tr>
<tr>
<td>Back pain</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Heart burn</td>
<td>49</td>
<td>24.5</td>
</tr>
<tr>
<td>Jaundice</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Fever</td>
<td>22</td>
<td>11</td>
</tr>
</tbody>
</table>

Fatty food intolerance stayed at 7.5% at six months (BR=0.87). Despite the persistence of some symptoms, the P value remained <0.05 (significant) in all cases. De novo appearance of symptoms was noted in few patients (Table 2).

Table 2. Pre-operative and postoperative symptoms and benefit ratios (N=200).

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Preop*</th>
<th>1 month Postop</th>
<th>3 month Postop</th>
<th>6 month Postop</th>
<th>Denovo</th>
<th>BR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>197 (98.5)</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>0 (0)</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nausea</td>
<td>140 (70)</td>
<td>35 (17.5)</td>
<td>24 (12)</td>
<td>19 (9.5)</td>
<td>4(2)</td>
<td>0.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vomiting</td>
<td>50 (25)</td>
<td>4 (2)</td>
<td>0</td>
<td>0</td>
<td>0(0)</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>116 (83)</td>
<td>75 (37.5)</td>
<td>73 (36.5)</td>
<td>76 (38.5)</td>
<td>5(2.5)</td>
<td>0.34</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Fatty Food Intolerance</td>
<td>114 (57)</td>
<td>16 (8)</td>
<td>15 (7.5)</td>
<td>15 (7.5)</td>
<td>4(2)</td>
<td>0.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Flatulence</td>
<td>42 (21)</td>
<td>34 (17)</td>
<td>32 (16)</td>
<td>26 (13)</td>
<td>5(2.5)</td>
<td>0.38</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Back pain</td>
<td>12 (6)</td>
<td>4 (2)</td>
<td>3(1.5)</td>
<td>3 (1.5)</td>
<td>2(1)</td>
<td>0.57</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Heart burn</td>
<td>49 (24.5)</td>
<td>18 (9)</td>
<td>19 (9.5)</td>
<td>19 (9.5)</td>
<td>2(1)</td>
<td>0.58</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*Figures in parentheses represent percentages

None of the patients had more than two symptoms persisting in the postoperative period. Eight percent developed new symptoms in the post-operative period ranging from dyspepsia (2.5%), flatulence (2.5%), fatty food intolerance (2%), and heart burn (1%). Overall, 93% patients were satisfied with the symptomatic outcome of the operation.
DISCUSSION
The results indicate that a major proportion of pre-operative symptoms associated with gall stones were relieved after cholecystectomy. However, as reported earlier, the impact on individual symptoms remains variable. 62% of patients had complete relief of preoperative symptoms, 38% had only one symptom persisting and 22% had two symptoms persisting after 6 months of follow-up. A previous study reported similar effects of cholecystectomy. Eight percent patients had de novo development of one or more new symptoms, a phenomenon well documented in the literature. Analysis of symptom specificity has demonstrated that colicky pain in the right upper quadrant (biliary colic) associated with gallstones is completely relieved by cholecystectomy. Similarly, nausea, vomiting and heartburn are symptoms related to gall stones and are mostly relieved by removal of gall bladder. Our study found similar results. The resolution of heartburn after cholecystectomy is significant as this suggests that the symptom usually attributed to gastro-oesophageal reflux can be a manifestation of gallstone disease.

Several studies have reported that dyspepsia and fatty food intolerance are only partly relieved by cholecystectomy, raising doubts whether they are directly related to the gallstones. In the present study, we found that the fatty food intolerance was markedly improved after surgery. However, dyspepsia still persisted in 38.5% of patients at 6 months of follow-up and 5 patients (2.5%) developed this symptom de novo in the postoperative period.

Removal of gallbladder is associated with several physiological changes in the upper GIT that may account for the persistence or appearance of new symptoms in these patients after surgery. Cholecysto-sphincter of Oddi reflex, cholecysto-antral reflex and cholecysto-oesophageal reflexes are all disrupted. Similarly, a number of local upper GI hormonal changes occur, leading to gastritis, alkaline duodeno-gastric reflux and gastro-esophageal reflux. These changes form the potential basis of persistence or de novo appearance of symptoms in the post-operative period known as post-cholecystectomy syndrome.

Other abdominal symptoms such as flatulence, bloating or back pain were partly relieved in our patients. These are not directly related to gallstone disease. Except one, most
studies have reported that the long term symptomatic outcome is not influenced by the surgical access used for cholecystectomy.\textsuperscript{2,15} However, chances of reporting adverse outcome are more in patients having developed a complication after surgery.\textsuperscript{15,16} This bias was removed in our study where only non-complicated cases were included for interview. Attempts at defining clinical indices or scores of pre-operative symptoms which are definitely improved after cholecystectomy have met with limited success,\textsuperscript{5,17} even after multivariate analyses.\textsuperscript{18} Despite the persistence or de novo appearance of symptoms in the post-operative period, 93\% of patients felt satisfied with the outcome of surgery. Studies have indicated that the patients felt that these problems or symptoms were not interfering in their routine of life as much as the actual problems due to cholelithiasis in the preoperative period.\textsuperscript{2,19} Moreover, there is a placebo effect of surgery on the overall wellbeing of the patients who tend to ignore the minor abdominal problems after surgery. **CONCLUSION** Cholecystectomy appears to relieve most of the symptoms of gall stone disease. Biliary pain, nausea, vomiting and fatty food intolerance had better outcome compared to dyspepsia, flatulence and heart burn. Some patients tend to develop de novo symptoms in the post-operative period. Despite the persistence or appearance of new symptoms, most of the patients feel satisfied with the outcome of surgery.

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